

# Theoretical and Numerical analysis of immobilised $\alpha$ -chymotrypsin under kinetic control

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**Abstract:** In this paper, a mathematical model for immobilized  $\alpha$ -chymotrypsin under kinetic control steady-state conditions is discussed. The model is based on diffusion equations containing a non-linear term related to the reaction processes. Analytical expressions for concentrations are derived using Modified Adomian decomposition method. Satisfactory agreement is obtained in the comparison of approximate analytical solution and numerical simulation.

**Keywords:** Kinetically controlled peptide synthesis, Nucleophile, Internal diffusion and reaction, Non-linear equations, Modified Adomian decomposition method.

## I. INTRODUCTION

In recent years, concentration is devoted to enzymes and biocatalysts, particularly monophasic organic solvents [1-5]. Enzymes are normally tightly packed in cellular organelles or in enzyme cascades thus enabling catalytic processes to take place precisely when and where they are needed [6]. Since enzymes are usually insoluble in these systems, unless otherwise conveniently engineered, these are heterogeneous catalytic systems. When comparing the activity of enzymes various organic solvents, it is important to ensure that the roles of external and internal diffusion non-aqueous enzymatic systems do not change for different solvents [7].

These problems may be solved by the use of immobilized enzymes. Immobilization often stabilizes structure of the enzymes, thereby allowing their applications even under harsh environmental conditions [8, 9]. Many predictions of biocatalyst behavior are based on relatively simple physical or chemical interpretations, sometimes combined with knowledge from biocatalysts in aqueous systems. Thermodynamic approaches that consider the distribution of components among the various phases, and their solvation in the bulk (i.e. organic) phase have proved to be particularly useful [10, 11]. A number of applications for enzymes in organic solvents have been developed in chemical processing (particularly for the synthesis of optically active intermediates), food-related conversions and analyses [12].

The study of simultaneous diffusion and reaction is important in order to optimize the catalytic system, which is confirmed by the large number of publications dealing with description and mathematical modeling of this phenomenon [13–20]. Built a model to describe the action of immobilized  $\alpha$ -chymotrypsin synthesizing di- or tripeptides in acetonitrile medium under kinetic control [21].

To the best of our knowledge, there are no analytical solutions reported for the molar concentrations of acyl donor and nucleophile. In this paper, we have derived the new analytical expression of concentration of acyl donor and nucleophile. Also we have provided the simple expression of rate consumption for each of the substrates. In addition our analytical results of the molar concentrations are compared with the numerical simulations using Matlab program.

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### II. MATHEMATICAL MODELING

In acetonitrile medium under kinetic control, the action of  $\alpha$ -chymotrypsin synthesizing di- or tripeptides can be expressed by the following enzyme-catalyzed reactions [21]:

Formation of product:



Hydrolysis of acyl donor:



The rate equations of peptide and hydrolysis product from the equation. The above intrinsic kinetics can written as follows [21]:

$$\frac{d^2[AcD]}{dr^2} + \frac{2}{r} \frac{d[AcD]}{dr} = \frac{1}{D_{Aeff}} \frac{(k_{Synth}[Nuc] + k_{Hydr})[AcD][E_0]}{k_N + [Nuc]} \quad (3)$$

$$\frac{d^2[Nuc]}{dr^2} + \frac{2}{r} \frac{d[Nuc]}{dr} = \frac{1}{D_{Neff}} \frac{k_{Synth}[Nuc][AcD][E_0]}{k_N + [Nuc]} \quad (4)$$

where  $[AcD]$  and  $[Nuc]$  are the molar concentrations of acyl donor and nucleophile,  $D_{Aeff}$  and  $D_{Neff}$  are the effective diffusion coefficient of acyl donor and nucleophile and  $E_0$  is the amount of enzyme,  $k_{Synth}$ ,  $k_{Hydr}$  and  $k_N$  are the kinetic constants. The boundary conditions for the above system of nonlinear reaction-diffusion equations are as follows [21]:

$$r = 0; \quad \frac{d[AcD]}{dr} = 0, \quad \frac{d[Nuc]}{dr} = 0 \quad (5)$$

$$r = R; \quad [AcD] = [AcD]_B, \quad [Nuc] = [Nuc]_B \quad (6)$$

where  $R$  is the particle radius,  $[AcD]_B$  and  $[Nuc]_B$  are the bulk molar concentrations of acyl donor and nucleophile in the reaction stream.

The initial rate of consumption of each of the substrates is given by

$$Rate_A = \frac{4\pi R^2}{M_p} D_{Aeff} \left. \frac{d[AcD]}{dr} \right|_{r=R} \quad (7)$$

$$Rate_N = \frac{4\pi R^2}{M_p} D_{Neff} \left. \frac{d[Nuc]}{dr} \right|_{r=R} \quad (8)$$

By introducing the following dimensionless parameters

$$U = \frac{[AcD]}{[AcD]_B}; \quad V = \frac{[Nuc]}{[Nuc]_B}; \quad x = \frac{r}{R}; \quad \gamma_1 = \frac{R^2 k_{Hydr} [AcD]_B E_0}{D_{Aeff} k_N}; \quad \alpha_1 = \frac{k_{Synth} [Nuc]_B}{k_{Hydr}}; \quad \alpha_2 = \frac{[Nuc]_B}{k_N};$$

$$\gamma_2 = \frac{R^2 k_{Synth} [AcD]_B [Nuc]_B E_0}{D_{Neff} k_N}$$

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The Eqs. (3) and (4) reduced to the following forms:

$$\frac{d^2U}{dx^2} + \frac{2}{x} \frac{dU}{dx} = \frac{\gamma_1 U(1 + \alpha_1 V)}{1 + \alpha_2 V} \tag{9}$$

$$\frac{d^2V}{dx^2} + \frac{2}{x} \frac{dV}{dx} = \frac{\gamma_2 UV}{1 + \alpha_2 V} \tag{10}$$

The boundary conditions in dimensionless form are as follows:

$$\frac{dU}{dx} = 0, \frac{dV}{dx} = 0 \quad \text{at } x = 0 \tag{11}$$

$$U = 1, V = 1 \quad \text{at } x = 1 \tag{12}$$

The dimensionless form of rate consumption are as follows:

$$\frac{Rate_A}{\mu} = \left. \frac{dU}{dx} \right|_{x=1} \tag{13}$$

$$\frac{Rate_N}{\eta} = \left. \frac{dV}{dx} \right|_{x=1} \tag{14}$$

where  $\mu = \frac{4\pi R^2}{M_p} D_{Aeff} [AcD]_B$  and  $\eta = \frac{4\pi R^2}{M_p} D_{Neff} [Nuc]_B$  (15)

**III. ANALYTICAL DETERMINATION OF THE CONCENTRATIONS OF OF THE ACYL DONOR AND NUCLEOPHILE UNDER STEADY-STATE**

The Adomian decomposition method (ADM) is a creative and effective method for exactly solving the differential equations of various kinds. It is important to note that a large amount of research work has been devoted to the application of the ADM to a wide class of linear and nonlinear, ordinary or partial differential equations. The ADM decomposes a solution into an infinite series which converges rapidly to the exact solution. The convergence of the ADM has been investigated by a number of authors [22-27]. In order to solve the boundary value problem, Eq. 9–12, we used the Adomian decomposition method.

The basic principle of this method is described in Appendix A. Detailed derivations of the dimensionless concentrations  $U$  and  $V$  of the acyl donor and nucleophiles are described in Appendix B. As a result, we have obtained

$$U(x) = 1 - \frac{1}{36} [A - 6l_1] (x^2 - 1) + \frac{1}{120} A (x^4 - 1) \tag{16}$$

$$V(x) = 1 - \frac{1}{36} [B - 6m_1] (x^2 - 1) + \frac{1}{120} B (x^4 - 1) \tag{17}$$

where

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$$l_1 = \gamma_1 \frac{1 + \alpha_1}{1 + \alpha_2}, m_1 = \frac{\gamma_2}{1 + \alpha_2} \text{ and } A = l_1^2 + \frac{m_1^2}{\gamma_2} (\gamma_1 \alpha_1 - \alpha_2 l_1), B = m_1 \left( \frac{m_1^2}{\gamma_2} + l_1 \right) \quad (18)$$

The Equations (16) and (17) represent the new analytical expression of concentration of acyl donor and nucleophile for all possible values of parameters. The analytical expressions of the rate consumption of each substrate are as follows:

$$\frac{\text{Rate}_A}{\mu} = -\frac{1}{18} [A - 6l_1] + \frac{1}{30} A \quad (19)$$

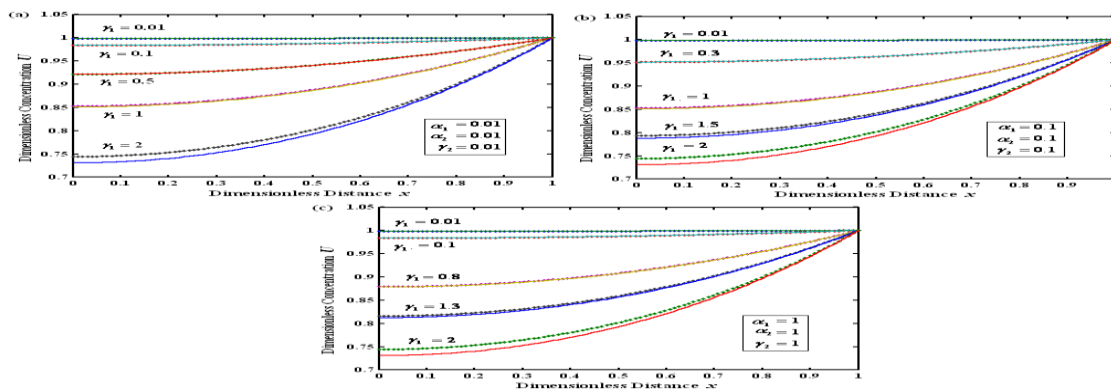
$$\frac{\text{Rate}_B}{\mu} = -\frac{1}{18} [B - 6m_1] + \frac{1}{30} B \quad (20)$$

### IV. SIMULATION

The diffusion equations (9) and (10) for the boundary conditions (11) and (12) are solved numerically. We have used the function pde4 in MATLAB software to solve numerically the initial-boundary value problems for the nonlinear differential equations. This numerical solution is compared with our analytical results in Figs. (1-3) and (4-5). Upon comparison, it gives a satisfactory agreement for all possible values of the dimensionless parameters,  $\alpha_1, \alpha_2, \gamma_1$  and  $\gamma_2$ . The MATLAB program is also given in Appendix C.

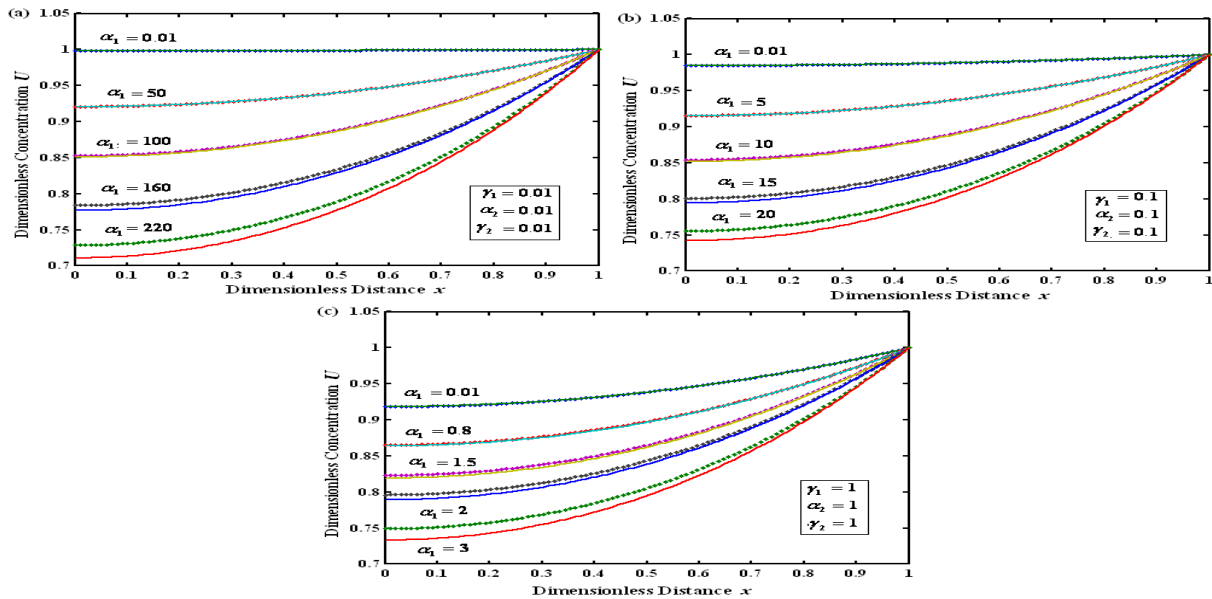
### V. RESULT AND DISCUSSION

In fig 1-3, Normalized concentration profile of substrate  $U$  for various values of the diffusion parameter  $\gamma_1$  and  $\alpha_1$  is plotted using Eqn. (16). From these figures it is observed that the value of concentration is approach to 1 ( $U \approx 1$ ) or uniform for all small values of the parameters  $\alpha_1, \alpha_2$  and  $\gamma_2$ . When increasing the value of diffusion parameter  $\gamma_1$  and  $\alpha_1$ , the concentration decreases. Normalized concentration profile of substrate  $V$  for various values of the diffusion parameter  $\gamma_1$  and  $\gamma_2$  is plotted using Eqn. (17).

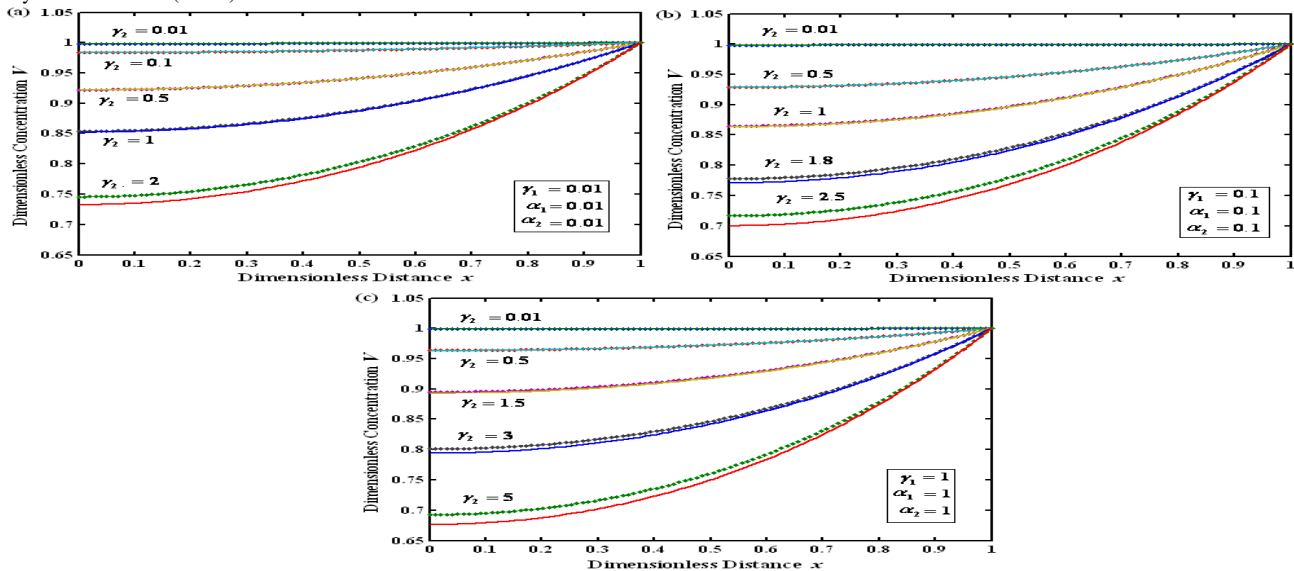


**Fig. 1.** Plot of dimensionless concentration of acyl donor  $U$  versus dimensionless distance  $x$ . The concentration was computed for various values of the dimensionless parameters  $\gamma_1$  when the values of  $\alpha_1, \alpha_2$  and  $\gamma_2$  are fixed. The curves are plotted using equation (16). (—) denotes the analytical results and (•••) denotes the numerical simulations.

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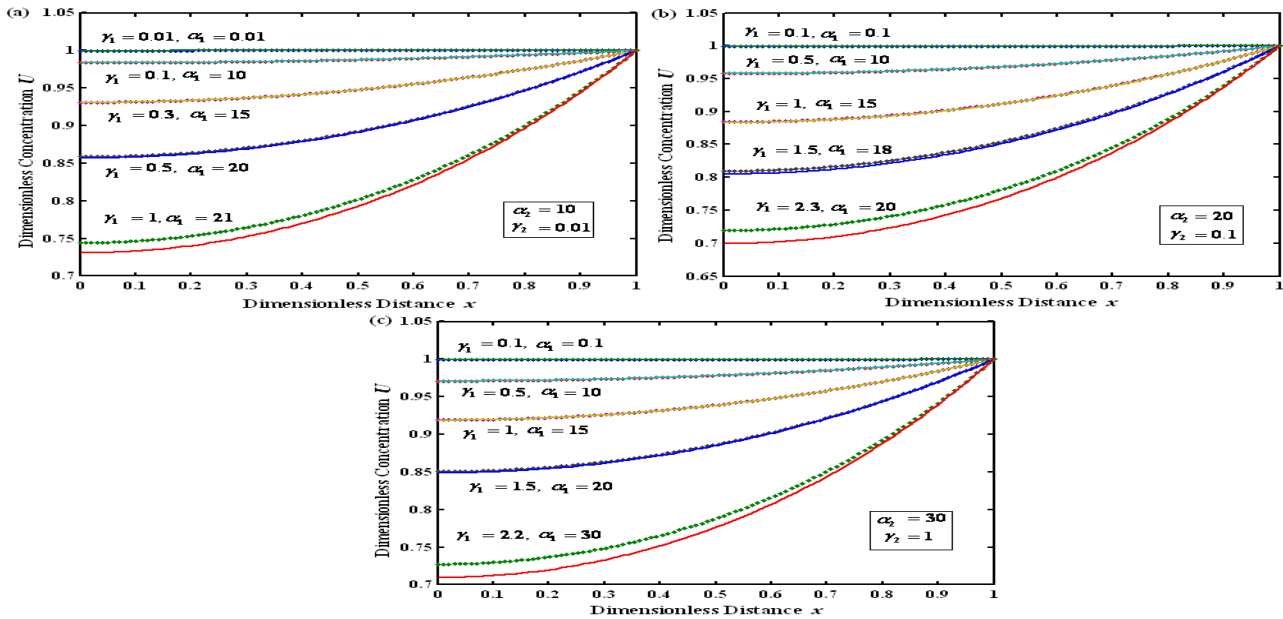
**Fig. 2.** Plot of dimensionless concentration of acyl donor  $U$  versus dimensionless distance  $x$ . The concentration was computed for various values of the dimensionless parameters  $\alpha_1$  and for some fixed values of  $\gamma_1$ ,  $\alpha_2$  and  $\gamma_2$ . The Scurves are plotted using equation (16). (—) denotes the analytical results and (•••) denotes the numerical simulations.



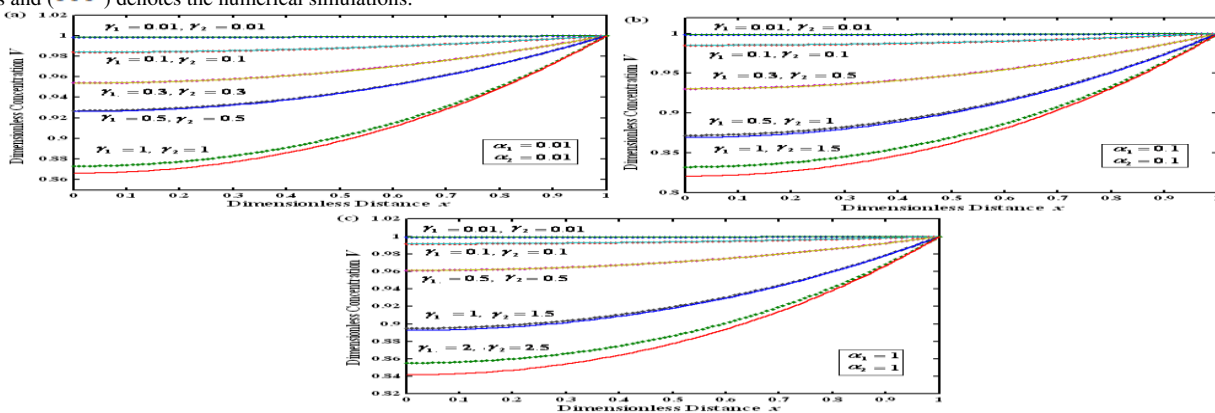
**Fig. 3.** Plot of dimensionless concentration of acyl donor  $U$  versus dimensionless distance  $x$ . The concentration was computed for various values of the dimensionless parameters  $\gamma_1$ ,  $\alpha_1$  and for some fixed values of  $\alpha_2$  and  $\gamma_2$ . The curves are plotted using equation (16). (—) denotes the analytical results and (•••) denotes the numerical simulations.

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In fig. 4-5, it is observed that the value of concentration is uniform for all small values of the parameters  $\alpha_1$  and  $\alpha_2$ . When increasing the value of diffusion parameter  $\gamma_2$ , the concentration decreases. It is evident that the concentration is high for minimum values of the diffusion parameters. Concentration decreases as the values of the diffusion parameters increases.



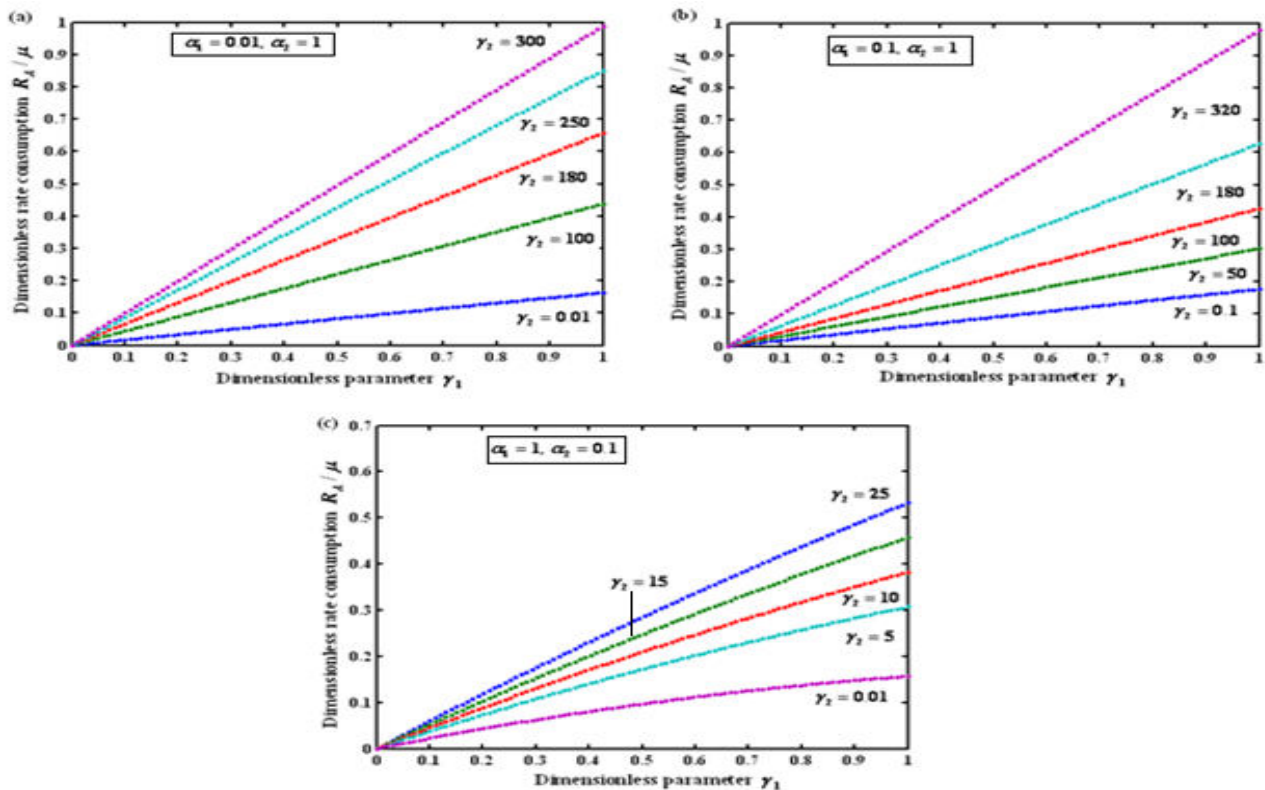
**Fig. 4.** Plot of dimensionless concentration of nucleophiles  $V$  versus dimensionless distance  $X$ . The concentration was computed for various values of the dimensionless parameters  $\gamma_2$  and for some fixed values  $\gamma_1$ ,  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (17). (—) denotes the analytical results and (•••) denotes the numerical simulations.



**Fig. 5.** Plot of dimensionless concentration of nucleophiles  $V$  versus dimensionless distance  $X$ . The concentration was computed for various values of the dimensionless parameters  $\gamma_1$  and  $\gamma_2$  and for some fixed values of  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (17). (—) denotes the analytical results and (•••) denotes the numerical simulations.

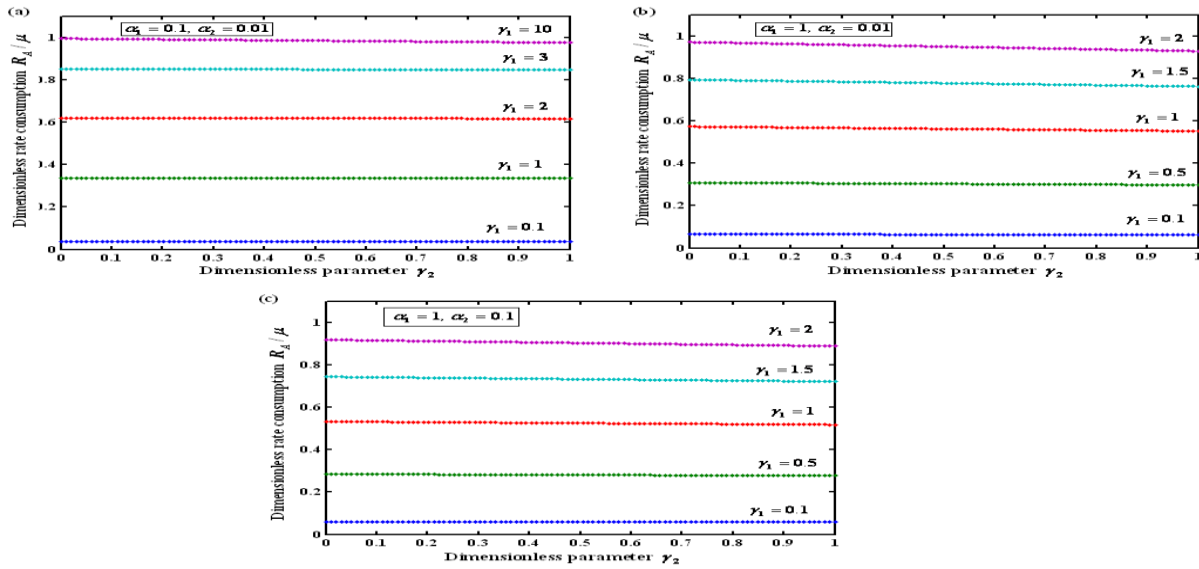
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Figs. 6 and 7, shows the dimensionless rate of consumptions  $R_A / \mu$  versus dimensionless parameters  $\gamma_1$  and  $\gamma_2$  respectively for the substrate  $U$ . Figs. 8 and 9, represents the dimensionless rate consumptions  $R_N / \eta$  versus dimensionless parameters  $\gamma_1$  and  $\gamma_2$  respectively for the substrate  $V$ . From fig.6 and 8, it is clear that the rate consumption increases as the values of  $\gamma_1$  increases for some fixed values of  $\alpha_1$  and  $\alpha_2$ . In fig. 7 and 9, it is clear that the rate consumption is linearly constant for all values of the parameter  $\gamma_1$  as the value of dimensionless parameter  $\gamma_2$  increases. Also it is evident that the rate consumption increases, when the value of  $\gamma_1$  increases.

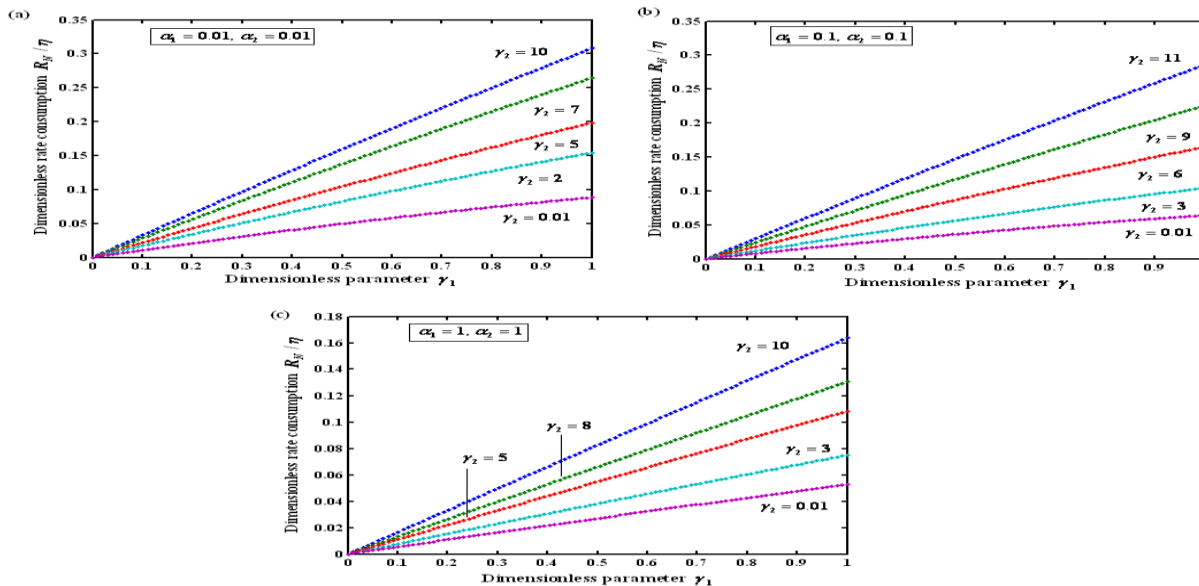


**Fig. 6.** Plot of dimensionless rate consumption  $R_A / \mu$  versus dimensionless parameter  $\gamma_1$ . The rate consumption was computed for various values of the dimensionless parameters  $\gamma_2$  and for some fixed values of  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (19). (•••) denotes the analytical result.

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**Fig. 7.** Plot of dimensionless rate consumption  $R_A / \mu$  versus dimensionless parameter  $\gamma_2$ . The rate consumption was computed for various values of the dimensionless parameters  $\gamma_1$  and for some fixed values of  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (19). (●●●) denotes the analytical results.



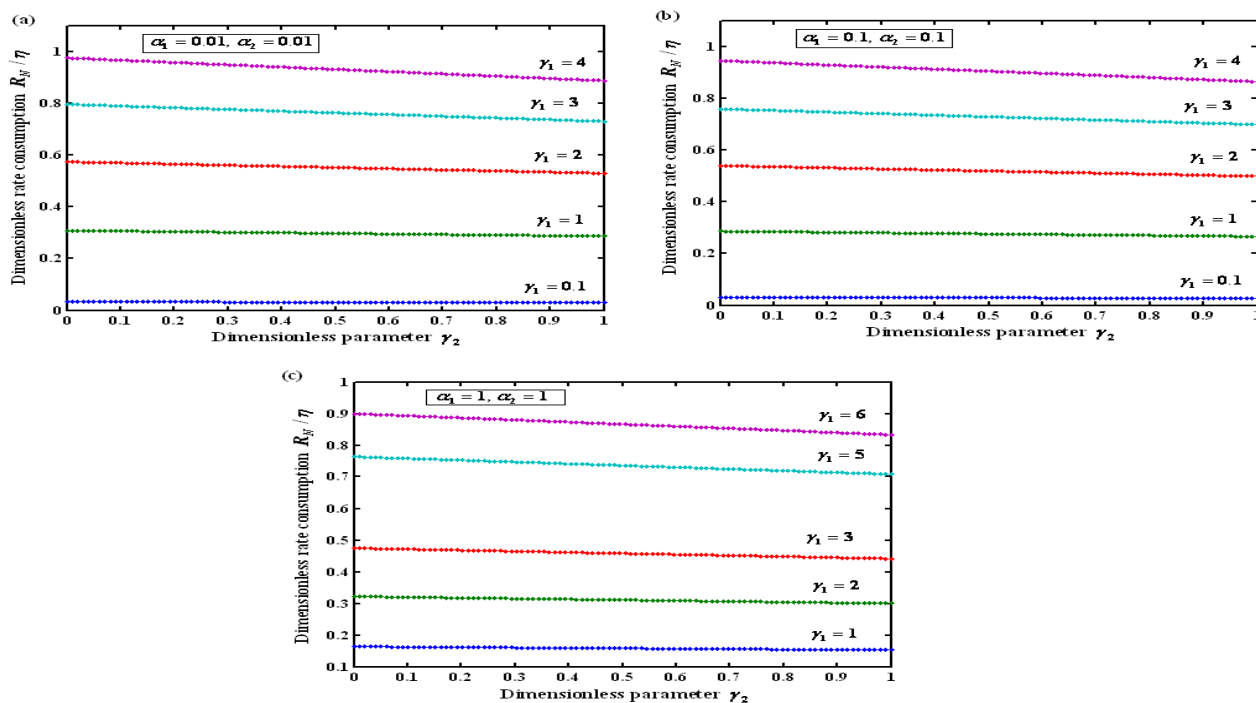
**Fig. 8.** Plot of dimensionless rate consumption  $R_N / \eta$  versus dimensionless parameter  $\gamma_1$ . The rate consumption was computed for various values of the dimensionless parameters  $\gamma_2$  and for some fixed values of  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (20). (●●●) denotes the analytical results.



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**Fig. 9.** Plot of dimensionless rate consumption  $R_N/\eta$  versus dimensionless parameter  $\gamma_2$ . The rate consumption was computed for various values of the dimensionless parameters  $\gamma_1$  and for some fixed values of  $\alpha_1$  and  $\alpha_2$ . The curves are plotted using equation (20). (•••) denotes the analytical results.

**VI. CONCLUSIONS**

In this work, we obtained analytical expressions of concentration of acyl donor and nucleophile for all possible values of dimensionless parameters. The closed analytical expressions of concentrations are obtained using modified Adomian decomposition method. Furthermore, on the basis of the outcome of this work, it is possible to calculate the approximate amounts of rate consumption used for immobilized  $\alpha$ -chymotrypsin catalyzed peptide synthesis in acetonitrile medium for all possible values of the parameters. This method is an extremely simple method and it is also a promising method to solve other non-linear equations. The information gained from this theoretical model can be useful for the kinetic analysis of the experimental results and the product distribution.

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**APPENDIX A: BASIC CONCEPT OF MODIFIED ADOMIAN DECOMPOSITION METHOD**

Consider the nonlinear differential equation in the form [23]:

$$y'' + \frac{2n}{x} y' + \frac{n(n-1)}{x^2} y + F(x, y) = g(x); n \geq 0 \tag{A.1}$$

with initial condition

$$y(0) = A, y'(0) = B \tag{A.2}$$

where  $F(x, y)$  is a real function,  $g(x)$  is the given function and  $A$  and  $B$  are constants. We propose the new differential operator, as below

$$L = x^{-n} \frac{d^2}{dx^2} x^n y \tag{A.3}$$

So, the problem (A.1) can be written as,

$$Ly = g(x) - F(x, y). \tag{A.4}$$

The inverse operator  $L^{-1}$  is therefore considered a two-fold integral operator, as below.

$$L^{-1}(\cdot) = x^{-n} \int_0^x \int_0^x x^n (\cdot) dx dx \tag{A.5}$$

Applying  $L^{-1}$  of (A.5) to the first three terms  $y'' + \frac{2n}{x} y' + \frac{n(n-1)}{x^2} y$  of Equation (A.1), we find

$$\begin{aligned} L^{-1}\left(y'' + \frac{2n}{x} y' + \frac{n(n-1)}{x^2} y\right) &= x^{-n} \int_0^x \int_0^x x^n \left(y'' + \frac{2n}{x} y' + \frac{n(n-1)}{x^2} y\right) dx dx \\ &= x^{-n} \int_0^x (x^n y' + nx^{n-1} y) dx \\ &= y - y(0) \end{aligned}$$

By operating  $L^{-1}$  on (A.4), we have

$$y(x) = A + L^{-1} g(x) - L^{-1} F(x, y) \tag{A.6}$$

The modified Adomian decomposition method introduce the solution  $y(x)$  and the nonlinear function  $F(x, y)$  by infinity series

$$y(x) = \sum_{n=0}^{\infty} y_n(x), \tag{A.7}$$

$$\text{and } F(x, y) = \sum_{n=0}^{\infty} A_n \tag{A.8}$$

where the components  $y_n(x)$  of the solution  $y(x)$  will be determined recurrently and the Adomian polynomials  $A_n$  of  $F(x, y)$  are evaluated [14-15] using the formula

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$$A_n(x) = \frac{1}{n!} \frac{d^n}{d\lambda^n} N \left( \sum_{n=0}^{\infty} (\lambda^n y_n) \right) \Big|_{\lambda=0} \tag{A.9}$$

By substituting (A.7) and (A.8) into (A.6),

$$\sum_{n=0}^{\infty} y_n(x) = A + L^{-1} g(x) - L^{-1} \sum_{n=0}^{\infty} A_n \tag{A.10}$$

Through using modified Adomian decomposition method, the components  $y_n(x)$  can be determined as

$$y_0(x) = A + L^{-1} g(x) \tag{A.11}$$

$$y_{n+1}(x) = -L^{-1}(A_n), n \geq 0$$

which gives

$$y_0(x) = A + L^{-1} g(x)$$

$$y_1(x) = -L^{-1}(A_0)$$

$$y_2(x) = -L^{-1}(A_1) \tag{A.12}$$

$$y_3(x) = -L^{-1}(A_2)$$

...

From (A.9) and (A.12), we can determine the components  $y_n(x)$ , and hence the series solution of  $y(x)$  in (A.7) can be immediately obtained.

**APPENDIX B: SYSTEMATIC SOLUTION FOR THE CONCENTRATIONS OF ACYL DONOR AND NUCLEOPHILE**

The solution of Eqns. (9) and (10) allows us to predict the concentration of acyl donor and nucleophile. We write Eqns. (9) and (10) in the operator form and derive its general solution using Modified Adomian decomposition method. The operator form is

$$L \begin{bmatrix} U(x) \\ V(x) \end{bmatrix} = N \begin{bmatrix} U(x) \\ V(x) \end{bmatrix} = \begin{bmatrix} \gamma_1(1 + \alpha_1 V(x)) \\ \gamma_2 V(x) \end{bmatrix} \frac{U(x)}{1 + \alpha_2 V(x)} \tag{B.1}$$

where  $L = x^{-1} \frac{d^2}{dx^2} x$ . Applying the inverse operator  $L^{-1}$  to both sides of Eqn. (B.1) yields, in agreement with Eqs. (A.6), (A.8) and (A.10).

$$\begin{aligned} \begin{bmatrix} U(x) \\ V(x) \end{bmatrix} &= \sum_{n=0}^{\infty} \begin{bmatrix} U_n(x) \\ V_n(x) \end{bmatrix} = \begin{bmatrix} P_U \\ P_V \end{bmatrix} x + \begin{bmatrix} Q_U \\ Q_V \end{bmatrix} + L^{-1} \begin{bmatrix} \gamma_1(1 + \alpha_1 V(x)) \\ \gamma_2 V(x) \end{bmatrix} \frac{U(x)}{1 + \alpha_2 V(x)} \\ &= \begin{bmatrix} P_U \\ P_V \end{bmatrix} x + \begin{bmatrix} Q_U \\ Q_V \end{bmatrix} + L^{-1} \sum_{n=0}^{\infty} \begin{bmatrix} A_{n,U} \\ A_{n,V} \end{bmatrix} \end{aligned} \tag{B.2}$$

where  $P_U, P_V, Q_U$  and  $Q_V$  are the integration constant and the Adomian polynomial coefficients  $A_{n,i}(x)$  ( $i = U, V$ ) can be obtained using Eq. (A.9). By equating the terms of Eq. (B.2) and using the boundary conditions (11) and (12), we get

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$$\begin{bmatrix} U_0(x) \\ V_0(x) \end{bmatrix} = \begin{bmatrix} P_U \\ P_V \end{bmatrix} x + \begin{bmatrix} Q_U \\ Q_V \end{bmatrix} = \begin{bmatrix} 1 \\ 1 \end{bmatrix} \tag{B.3}$$

The first two Adomian polynomial coefficients  $A_{n,i}(x)$  ( $i = U, V$ ) are

$$\begin{bmatrix} A_{0,U} \\ A_{0,V} \end{bmatrix} = \begin{bmatrix} \gamma_1(1 + \alpha_1) \\ \gamma_2 \end{bmatrix} \frac{1}{1 + \alpha_2} = \begin{bmatrix} l_1 \\ m_1 \end{bmatrix} \tag{B.4}$$

$$\begin{bmatrix} A_{1,U} \\ A_{1,V} \end{bmatrix} = \begin{bmatrix} l_1 U_1(x) + \frac{m_1}{\gamma_2} (\gamma_1 \alpha_1 - \alpha_2 l_1) V_1(x) \\ m_1 U_1(x) + \frac{m_1^2}{\gamma_2} V_1(x) \end{bmatrix} = \frac{1}{6} \begin{bmatrix} A(x^2 - 1) \\ B(x^2 - 1) \end{bmatrix} \tag{B.5}$$

where  $A = l_1^2 + \frac{m_1^2}{\alpha_4} (\gamma_1 \alpha_1 - \alpha_2 l_1)$ ,  $B = m_1 (\frac{m_1^2}{\gamma_2} + l_1)$  (B.6)

From the above equations we obtain  $U_1(x), V_1(x)$  and  $U_2(x), V_2(x)$  as follows:

$$\begin{bmatrix} U_1(x) \\ W_1(x) \end{bmatrix} = L^{-1} \begin{bmatrix} A_{0,U} \\ A_{0,W} \end{bmatrix} = \frac{(x^2 - 1)}{6} \begin{bmatrix} l_1 \\ m_1 \end{bmatrix} \tag{B.7}$$

$$\begin{bmatrix} U_2(x) \\ W_2(x) \end{bmatrix} = L^{-1} \begin{bmatrix} A_{1,U} \\ A_{1,W} \end{bmatrix} = \frac{1}{6} \begin{bmatrix} A \left( \frac{x^4 - 1}{20} - \frac{x^2 - 1}{6} \right) \\ B \left( \frac{x^4 - 1}{20} - \frac{x^2 - 1}{6} \right) \end{bmatrix} \tag{B.8}$$

Adding Eqs. (B.3), (B.7) and (B.8) we obtain Eqns. (16) and (17) in the text.

**APPENDIX C**

The Matlab program to find the numerical solution of equations (9) and (10):

```
function pdex4
m = 2;
x = linspace(0,1);
t=linspace(0,100000);
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('u1(x,2)')
%-----
figure
```

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```

plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,2)')
% -----
function [c,f,s] = pdex4pde(x,t,u,DuDx)
c = [0; 0];
f = [1; 1] .* DuDx;
a1=2.2;a2=30;a3=30;a4=1;
F=-(a1*u(1)*(1+a2*u(2)))/(1+a3*u(2));
F1=-(a4*u(1)*u(2))/(1+a3*u(2));
s=[F; F1];
% -----
function u0 = pdex4ic(x)
u0 = [1;1];
% -----
function [pl,ql,pr,qr]=pdex4bc(xl,ul,xr,ur,t)
pl = [0;0];
ql = [1; 1];
pr = [ur(1)-1; ur(2)-1];
qr = [0; 0];

```

**APPENDIX D: NOMENCLATURE**

- $D_{Aeff}$  Effective diffusion coefficient of acyl donor ( $cm^2/s$ )
- $D_{Neff}$  Effective diffusion coefficient of nucleophile ( $cm^2/s$ )
- $[AcD]$  Concentration of acyl donor ( $mM$ )
- $[Nuc]$  Concentration of nucleophile ( $mM$ )
- $[Hyp]$  Concentration of hydrolysis product ( $mM$ )
- $[Pep]$  Concentration of peptide product ( $mM$ )
- $k_{Hydr}$  Kinetic constant ( $\mu mol min^{-1} mg CT^{-1}$ )
- $k_N$  Kinetic constant ( $mM$ )
- $k_{Synth}$  Kinetic constant ( $ml min^{-1} mg CT^{-1}$ )
- $E_0$  Amount of enzyme ( $mg min^{-1}$ )
- $LG$  Leaving group (ethanol or methanol)
- $[AcD]_B$  Molar concentration of acyl donor ( $mM$ )
- $[Nuc]_B$  Molar concentration of nucleophile ( $mM$ )
- $r$  Distance from the centre of the particle
- $R$  Particle radius ( $cm$ )